Evaluation of the Department of Defense Persian Gulf Comprehensive Clinical Evaluation Program

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Evaluation of the U.S. Department of Defense Persian Gulf Comprehensive Clinical Evaluation Program

Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

Division of Health Promotion and Disease Prevention

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Evaluation of the U.S. Department of Defense Persian Gulf Comprehensive Clinical Evaluation Program

EXECUTIVE SUMMARY

In July 1994, the U.S. Department of Defense (DoD) asked the Institute of Medicine (IOM) to establish a committee to evaluate its Comprehensive Clinical Evaluation Program (CCEP). Since their return from service in the Persian Gulf region during Operations Desert Shield and Desert Storm, some active-duty military personnel and veterans have reported a variety of health problems that they perceived to be associated with their service in that region. The DoD instituted the CCEP in June 1994 to evaluate and treat the health problems of these active-duty personnel. The DoD then asked the IOM committee to evaluate the protocol for the clinical evaluations and to comment on the interpretation of the CCEP results that have been obtained so far. In addition, the committee was asked to make recommendations relevant to the conduct of the clinical evaluations in the future and to the broader program of the DoD Persian Gulf health studies, if appropriate. The purpose of this report on the CCEP is to provide a comprehensive evaluation of the major issues that the committee has identified since its first meeting in October 1994.

The CCEP is a compassionate and comprehensive effort to address the clinical needs of thousands of active-duty personnel who served in the Persian Gulf War. The CCEP clinical protocol is a thorough, systematic approach to the diagnosis of a wide spectrum of diseases. A specific medical diagnosis or diagnoses can be reached for most patients by using the CCEP protocol. The DoD has made conscientious efforts to build consistency and quality assurance into this program at the many medical treatment facilities and regional medical

centers across the country. This nationwide effort was implemented relatively quickly. The committee commends the DoD for its efforts to provide high-quality medical care in the CCEP and the success it has achieved to date in developing the infrastructure necessary to efficiently contact, schedule, refer, and track thousands of patients through the system.

Of the first 10,020 CCEP patients, 37% were diagnosed with a psychiatric condition, most commonly depression or posttraumatic stress disorder. Many of the psychiatric diseases found in the CCEP population have both physical and psychological symptoms and manifestations. The IOM committee encourages the DoD to emphasize in its future reports that psychosocial stressors can produce physical and psychological effects that are as real and potentially devastating as physical, chemical, or biological stressors. The committee also encourages the DoD to emphasize that effective treatments exist for many of these psychiatric disorders.

There is currently no clinical evidence in the CCEP for a previously unknown, serious illness among Persian Gulf veterans. If there were a new or unique illness or syndrome among Persian Gulf veterans that could cause serious impairment in a high proportion of veterans at risk, it would probably be detectable in the population of 10,020 CCEP patients. On the other hand, if an unknown illness were mild or only affected a small proportion of veterans at risk, it might not be detectable in a case series, no matter how large. The DoD and the U.S. Department of Veterans Affairs (DVA) are sponsoring several large research studies that may provide more definitive answers as to whether there is a new, unique Persian Gulf Syndrome.

The CCEP was not, however, designed to answer epidemiological questions. Instead, it was designed as a medical evaluation and treatment program. In a recent report on 10,020 patients, the DoD compares the symptoms and diagnoses in the CCEP with the symptoms and diagnoses in several community-based and clinically based populations. The committee concludes that interpretations based on comparisons with other populations should be made with great caution and only with the explicit recognition of the limitations of the CCEP as a self-selected case series. The CCEP results do have considerable clinical utility, and they could be used to address many important questions from a descriptive perspective.

The results of the CCEP can and should be used for several purposes including (1) educating Persian Gulf veterans and the physicians caring for them, (2) improving the medical protocol itself, and (3) evaluating patient outcomes. The medical findings of the CCEP should be distributed promptly to all CCEP primary care physicians. The medical findings of the CCEP would also be of considerable value and interest to physicians in the DVA system and in the community.

The DoD should consider developing a comprehensive document for use in the CCEP that describes the potential physical, chemical, biological, and psychological stressors that were present in the Persian Gulf theater. If the CCEP physicians could obtain a clearer picture of the possible range of exposures, they might be able to counsel their patients more effectively.

Walter Reed Army Medical Center staff have developed the Specialized Care Center (SCC) for the evaluation, treatment, and rehabilitation of a small, select group of seriously impaired patients who have been referred from regional medical centers. The committee's review should be considered preliminary because the program is still early in its development. The committee believes that the DoD has taken a serious approach to the treatment and rehabilitation of these impaired patients who have treatable, chronic diseases. If the SCC program is successful in improving the health and functional status of its patients, perhaps the elements that are most effective in enabling the patients to cope with their symptoms could be identified. It might then be possible to disseminate some of these elements to the DoD medical treatment facilities, which are close to where the CCEP patients live and work.

INTRODUCTION

Since their return from service in the Persian Gulf region during Operations Desert Shield and Desert Storm, a number of active-duty military personnel and veterans have reported a variety of health problems that they perceived to be associated with their service in the Persian Gulf. In response to continuing concerns about these problems, the U.S. Department of Defense (DoD) instituted the Comprehensive Clinical Evaluation Program (CCEP) in June 1994. The program's main objective is the diagnosis and treatment of these active-duty military personnel who have medical complaints that they believe could be related to their service in the Persian Gulf. In the CCEP, each individual receives a comprehensive medical evaluation that is based on a standardized clinical protocol (DoD, 1995a).

In July 1994, Assistant Secretary of Defense for Health Affairs Stephen Joseph asked the Institute of Medicine (IOM) to convene a group of national medical and public health experts to complement the DoD's efforts with their analysis and to offer a channel for broader public comment and suggestions. In particular, the IOM committee was asked to evaluate the protocol for the clinical evaluations and to comment on the interpretation of the CCEP results that have been obtained so far. The committee was also asked to make recommendations relevant to the conduct of the clinical evaluations in the future and on the broader program of the DoD Persian Gulf health studies, if appropriate.

The DoD published its first results for the CCEP on December 13, 1994, in a report entitled Clinical Evaluation Program for Gulf War Veterans—Preliminary Status Report on the First 1,000 Patients (DoD, 1994). In April 1995, the DoD published its second report, entitled Clinical Evaluation Program for Gulf Veterans—Second Interim Report on 2,076 Participants (DoD, 1995b). The DoD also provided an unpublished draft DoD report to the IOM committee entitled Comprehensive Clinical Evaluation Program (CCEP) for Gulf War Veterans—Report on 10,020 Participants, dated June 7, 1995 (DoD, 1995c). The DoD then revised this report and released it to the public, with the same title, on August 1, 1995 (DoD, 1995d).

The IOM committee held its first meeting on October 24, 1994. It released its first interim report on the CCEP, which was based on the DoD presentations prepared for the first DoD report, on December 2, 1994 (IOM, 1994). The committee held its second meeting on March 10, 1995, during which several DoD clinicians discussed the results in its second report on 2,076 patients, as well as administrative aspects of the CCEP.

The IOM committee held its third meeting on June 8 and 9, 1995. The purpose of the meeting was to review the unpublished draft DoD report on 10,020 CCEP participants, dated June 7, 1995 (DoD, 1995c). In addition, several physicians who were involved with the CCEP gave presentations on the clinical results, and the committee made a site visit to the Specialized Care Center at the Walter Reed Army Medical Center in Washington, D.C. The committee released its second interim report on August 7, 1995, which commented on the unpublished draft DoD report and on the presentations at the June 8 and 9 meeting (IOM, 1995a).

The IOM committee held its fourth meeting on September 6, 1995, to draft and discuss the current report. The purpose of this report on the CCEP is to evaluate the major issues that the committee has identified since its first meeting in October 1994. The major topics of the two interim reports are incorporated here. The report consists of six sections on (1) the goals and procedures of the CCEP, (2) the implementation of the CCEP, (3) the analysis and interpretation of the results of the CCEP, (4) specific medical diagnoses, (5) use of the CCEP results for education, for improvements in the medical protocol, and for outcome evaluation, and (6) a summary of epidemiological research relevant to the CCEP.

GOALS AND PROCEDURES OF THE CCEP

Overview

The CCEP was developed by the DoD to provide a "systematic in-depth medical evaluation for all military health care beneficiaries who are experiencing illnesses which they believe may be related to Persian Gulf deployment" (DoD, 1995d). It was designed primarily as a clinical program to evaluate and treat the health problems of individuals. As a secondary goal, the DoD has released a series of reports that have summarized the results of the medical evaluations of the CCEP patients.

The CCEP and a similar U.S. Department of Veterans Affairs (DVA) protocol were implemented beginning in June 1994. Members of the service who are still on active duty or who are still active in the Reserves or National Guard request their medical evaluations from the DoD. Veterans who have already left the service, Reserves, or National Guard request their medical evaluations from DVA.

Phase I of the CCEP consists of a medical history, physical examination, and laboratory tests. These are comparable in scope and thoroughness to an evaluation conducted during an inpatient internal medicine hospital admission. Depending on the complexity of the patient's symptoms, this first phase is more comprehensive than the evaluation that a patient would usually receive in a primary care level outpatient work up (DoD, 1995a). All participants in the CCEP receive an evaluation by a primary care physician at their local medical treatment facility (MTF) and appropriate specialty consultations.

Patients are referred to Phase II for further specialty consultations at a regional medical center (RMC, a tertiary care hospital) when it is clinically indicated in the judgment of the primary care physician (DoD, 1995a). Phase II evaluations consist of targeted symptom-specific examinations, lab tests, and consultations, as mandated in the protocol. Both Phase I and Phase II are designed to be thorough for each individual patient and, at the same time, to be consistent among patients (DoD, 1995a).

Every MTF has a designated CCEP physician coordinator who is a board-certified family practitioner or internal medicine specialist. This physician coordinator is responsible for overseeing both the comprehensiveness and the quality of the Phase I exams. The CCEP activities at RMCs are coordinated by board-certified internal medicine specialists who oversee the program operations of the MTFs in their regions.

In March 1995, the DoD established the Specialized Care Center (SCC) at Walter Reed. The purpose of the SCC is to provide additional evaluation, treatment, and rehabilitation for patients who are suffering from chronic debilitating symptoms. A small select group of patients have been referred from

RMCs to the SCC for an intensive 3-week evaluation and treatment program which is designed to restore participants to a maximum state of health and fitness (DoD, 1995d).

All medical records from the CCEP are sent to the Navy Medical Information Management Center (NMIMC) in Bethesda, Maryland, to be coded and computerized for entry into the national CCEP database. At NMIMC, the reports undergo quality review for completeness, thoroughness, and accuracy of diagnostic coding (DoD, 1995d).

The CCEP was implemented in June 1994. By June 1, 1995, there were 16,729 requests for evaluations, and the DoD had been able to complete 13,150. The records for 10,020 of these evaluations had been reviewed for completeness, validated, and computerized (DoD, 1995d). The DoD has been able to develop the infrastructure necessary to efficiently contact, schedule, refer, and track thousands of patients through the system.

Committee Assessment of the Overall Goals and Procedures of the CCEP

The CCEP clinical protocol is a thorough, systematic approach to the diagnosis of a wide spectrum of diseases. A specific medical diagnosis or diagnoses can be reached for most patients by using the CCEP protocol. The DoD has made conscientious efforts to build consistency and quality assurance into this program at the many MTFs and RMCs across the country.

Overall, the committee is impressed with the quality of the design and the efficiency of the implementation of the clinical protocol, the considerable devotion of resources to this program, and the remarkable amount of work that has been accomplished in a year. The high professional standards, commitment, and diligence of the physicians involved in the CCEP at the RMCs were readily apparent at the three committee meetings. The committee commends the DoD for its efforts to provide high-quality medical care in the CCEP and the success that it has achieved to date in developing the infrastructure necessary to efficiently contact, schedule, refer, and track thousands of patients through the system.

Overall, the systematic, comprehensive set of clinical practice guidelines set forth in the CCEP are appropriate, and they have assisted physicians in the determination of specific diagnoses for thousands of patients across the country.

IMPLEMENTATION OF THE CCEP

Two areas that are involved with the implementation of the CCEP deserve attention. These are (1) referrals of patients from Phase I to Phase II, and (2) systematic guidelines for psychiatric referrals and the adequacy of psychiatric resources.

Referrals of Patients from Phase I to Phase II of the CCEP

At the time of the first committee meeting in October 1994, approximately 9,000 patients were registered in the CCEP, and the number was growing at the rate of more than 1,000 per month (IOM, 1994). Only about 20% of the patients were receiving a specific diagnosis in Phase I at the MTF level. About 80% of the patients were being referred to Phase II at the RMC level for the completion of their medical evaluations. This large patient load threatened to overwhelm the capacities of the RMCs.

Several relevant suggestions on the administration of the CCEP were made in the first IOM report, as follows:

One proposal that has emerged to deal with the large number of patients in the CCEP is to structure and revise the CCEP protocol and logistics so that a majority of patients would receive a final diagnosis by the staff of local MTFs in Phase I of the CCEP. Currently the majority of patients do not receive a final diagnosis until Phase II, yet some of these patients have straightforward medical problems such as migraine headaches or rheumatoid arthritis. If more diagnostic resources could be marshalled in Phase I, then perhaps many more final diagnoses could be reached at this stage. This major change would require the availability of substantial numbers of internists or family practitioners at MTFs to perform comprehensive evaluations. It would also require better, more consistent explanations to MTF physicians about the purposes and procedures of the CCEP. It would require regional medical center physicians to provide adequate quality assurance of MTF work-ups and timely feedback to MTF providers. . . .

Another option is to curtail diagnostic work-ups in patients with minor complaints, and who are not seriously disabled. Currently, patients who do not accept their initial diagnosis (for example, tension headaches or irritable bowel syndrome) can request a continued evaluation all the way through Phase II of the examination. Alternatively, it has been suggested that if a physician has made a

definitive diagnosis and appropriate treatment has been given, the evaluation would be concluded (IOM, 1994, p.6).

All of the committee's suggestions have subsequently been incorporated into the CCEP. On January 17, 1995, the DoD implemented several changes in the administrative procedures of the CCEP protocol (DoD, 1995a). In particular, the DoD set a goal that about 80% of patients would receive a definitive diagnosis at an MTF level and that only 20% would be referred to the RMC level (DoD, 1995a). For some patients, this change has required specialty consultations at the MTF, such as psychiatry or rheumatology, as well as advice from an RMC physician. These changes necessitated an enhanced quality control role by the RMC physician and prompt, appropriate feedback to the MTF physician. Another major change was that referral to Phase II was made on the basis of the clinical judgment of the primary care physician, and patients were no longer permitted to self-refer to an RMC.

These changes have improved the timeliness of patient scheduling and have reduced the backlog of patients waiting for the initiation or completion of their evaluations. Before February 1995, 28% of the CCEP patients were referred to an RMC; after that date, 4% were referred. Altogether, 83% of the first 10,020 CCEP evaluations were completed at Phase I and 17% were completed at Phase II (DoD, 1995c). The IOM committee encourages these efforts to provide more care at the primary care level, because they will enhance the continuity of care and will foster the establishment of an ongoing therapeutic relationship.

There is a subgroup of patients whose illnesses are difficult to diagnose and who should continue to be referred to Phase II at an RMC. The IOM committee believes that it is appropriate that the decision to refer to Phase II should be based on the clinical judgment of the primary care physician, which, in turn, would be dependent on the clarity of the patient's diagnoses and the feasibility of the proposed treatment program at the MTF level. The committee supports the DoD's goal of enhanced accessibility of RMC physicians to allow regular consultations with MTF primary care physicians on patients with more complex diagnoses.

Systematic Guidelines for Psychiatric Referrals and Adequacy of Psychiatric Resources

Several CCEP physicians have noted that there is a high degree of prevalence of psychosocial problems in the CCEP population and that there is a need for standardized guidelines for screening, assessing, evaluating, and treating patients. As discussed in more detail below, 37% of the first 10,020

patients in the CCEP had one or more psychiatric diagnoses—11% with depression and 5% with posttraumatic stress disorder (PTSD) (DoD, 1995d). Since the goal is for most patients to receive a definitive diagnosis in Phase I, but the psychiatric evaluation is mandated only for patients in Phase II, the committee recommends that the DoD develop explicit guidelines for the identification of patients in Phase I who would benefit from a psychiatric evaluation. This will help ensure adequate psychiatric resources for both the initial evaluation and long-term follow-up care.

Primary care physicians should be alerted to the relatively high degree of prevalence of these psychiatric disorders in this population. Two methods that have been proposed by RMC physicians to expedite the scheduling of psychiatric evaluations would be (1) the more frequent use of civilian psychiatrists and (2) consideration of using Ph.D.-level psychologists, as well as psychiatrists, when necessary.

ANALYSIS AND INTERPRETATION OF THE RESULTS OF THE CCEP

The DoD has released a series of reports that have summarized the results of the medical evaluations of the CCEP patients. The DoD has stated, "The large size of the CCEP cohort and the thoroughness of the CCEP examinations provide considerable clinical insight for understanding the nature of illnesses and health complaints experienced by this group of veterans" (DoD, 1995d). The DoD's most recent report, however, recommends caution in the generalization of the interpretation of the CCEP results: "However, self-selection of patients, differential eligibility, recall bias, inability to validate self-reported exposures, and lack of an appropriate control group limit the generalization of these findings to other Gulf War veterans" (DoD, 1995d).

Four major areas related to the analysis and interpretation of the results of the CCEP deserve attention: (1) the symptoms and diagnoses in the CCEP population; (2) clinical evidence for a new, unique Persian Gulf Syndrome; (3) the potential relationship of illnesses in some CCEP patients to service in the Persian Gulf; and (4) a comparison of the CCEP population with other populations.

Symptoms and Diagnoses in the CCEP Population

The CCEP patients report a very broad range of symptoms. The most recent DoD report on 10,020 participants summarizes the frequencies of the chief complaints and all complaints for these patients (DoD, 1995d). The most common symptoms are fatigue, joint pain, headache, rash/dermatitis, and

memory loss. Only two symptoms were given as the chief complaint by 10% or more of the patients: fatigue (11%) and joint pain (11%) (DoD, 1995d).

The median number of diagnoses per patient is three. The CCEP computer database records seven diagnoses. For a patient with three diagnoses, three different aspects of one organ system could be involved (e.g., three unrelated musculoskeletal problems) or three or more different organ systems (an extreme example would be diabetes, which is only one diagnosis but which affects several organs). The diagnoses in the first 10,020 CCEP patients are stratified by major International Classification of Disease, 9th edition (ICD-9), codes, in the recent DoD report (DoD, 1995d). There are only two major disease groups or organ systems in which 10% or more of the 10,020 patients have a primary diagnosis. The primary diagnosis is the one disease that the CCEP physician judges to be the most important or critical for each patient (DoD, 1995a). These two groups are psychological conditions (19%) and musculoskeletal conditions (16%). Similarly, there are only two major disease groups or organ systems in which 25% or more of the 10,020 patients have any diagnosis These are psychological conditions (37%) and (primary or secondary). musculoskeletal conditions (45%). Beyond this, the primary diagnoses among the first 10,020 patients do not appear to be concentrated in any single organ system.

Many different combinations of diagnoses exist among the 10,020 patients, and relatively few individuals have the same combinations of diseases. The CCEP physicians presented summaries of several case histories over the course of the three IOM meetings. Most of these individual cases had two or more discrete diagnoses, often in two or more different organ systems. Examples of two typical patient presentations might be (1) PTSD and asthma or (2) migraine headaches, hypothyroidism, and osteoarthritis of the left knee. In most of these cases, it was unlikely that the two or more diseases were different manifestations of the same underlying pathological process. The committee found no evidence that the DoD has been trying to avoid reaching a single "unifying" diagnosis when a plausible one was available. A "unifying" diagnosis is defined here as a single diagnosis that could explain most or all of a patient's symptoms.

One interpretation of the CCEP results is that the signs and symptoms in many patients can be explained by well-recognized conditions that are readily diagnosable and treatable. The committee concludes that this is a more likely interpretation than the interpretation that a high proportion of the CCEP patients are suffering from a unique, previously unknown "mystery disease." By providing more detailed information on specific diagnoses in its future reports, the DoD might help correct the impressions among the general public that exist about the high degree of prevalence of a "mystery disease" or a new, unique "Persian Gulf Syndrome."

In the medical history, the CCEP patients are asked about how many workdays they have lost because of illness in the last 90 days. Most patients (81%) reported that they had not missed any days of work because of illness during the 90 days before their initial evaluation. Few patients (7%) reported missing more than 1 week of work because of illness (DoD, 1995d). By this measure, most CCEP patients are not seriously impaired by their symptoms. However, it is likely that there are substantial disincentives for taking lengthy sick leave in the military, just as there are in civilian employment. In addition, the reported number of lost workdays may not always reflect more subtle functional impairments. Nonetheless, if these self-reported data on lost workdays are accurate, they can serve a useful sentinel role for significant impairment. It is unlikely that there is a high degree of prevalence of significant impairment among the CCEP population.

Disability processing actions in the Services' Physical Disability Processing Systems have been completed for 246 of the 10,020 CCEP patients (DoD, 1995c). The DoD has not provided any data about their diagnoses or their reasons for medical separation from the military. The committee recommends that the DoD investigate the diagnoses in this group of patients in future reports, as well as whether or not the disorders could have been caused or exacerbated by service in the Persian Gulf. Many other individuals who served in the Persian Gulf have left active service and, hence, are not eligible for the DoD's CCEP. Some of these veterans may have disabilities related or unrelated to their service in the Persian Gulf, and those with disabilities might be more likely to have left active service. For these reasons, the CCEP results should not be viewed as estimates of the prevalence of disability related to Persian Gulf service.

Clinical Evidence of a New, Unique Persian Gulf Syndrome

In the DoD report on 10,020 CCEP patients, a major conclusion is that "To date, the CCEP has identified no clinical evidence for a new or unique illness or syndrome among Persian Gulf veterans" (DoD, 1995d). The justification for this conclusion is as follows (DoD, 1995d):

DoD physicians have diagnosed a wide range of medical conditions commonly seen in general medical practice, but have found no clinical evidence for a unique illness among CCEP participants. The large number of patients participating in the CCEP, the thoroughness of the evaluations, and the clinical impressions of CCEP physicians are the primary basis for forming conclusions regarding the existence of a new or unique condition or syndrome.

The committee agrees that there is currently no clinical evidence in the CCEP of a previously unknown, serious illness among Persian Gulf veterans. If there were a new or unique illness or syndrome among Persian Gulf veterans that could cause serious impairment in a high proportion of veterans at risk, it would probably be detectable in the population of 10,020 CCEP patients. On the other hand, if an unknown illness were mild or affected only a small proportion of veterans at risk, it might not be detectable in a case series, no matter how large. For example, if some particular exposure in the Persian Gulf region could cause a small proportion of veterans to develop mild headaches, this would be difficult to detect. This is because mild headaches are common medical problems, and they are associated with many different risk factors.

Sophisticated statistical techniques, including cluster analysis, could be used to identify whether or not there are previously unidentified patterns of symptoms among the CCEP patients. If symptom patterns were identified, the patterns would have to be analyzed to determine whether the affected patients demonstrated characteristic physical abnormalities, lab test abnormalities, and risk factors that might suggest a new, unique syndrome. To be designated as a newly recognized disease, these patterns of physical abnormalities, lab test abnormalities, and risk factors would have to be objectively different from the patterns of well-recognized diseases. If it appears that there is a new, unique syndrome, an investigation of the association between this medical condition and exposure to physical and psychological stressors in the Persian Gulf would then be necessary. The committee encourages the DoD's plan to share the entire CCEP data set with qualified researchers outside of the DoD who might be able to undertake the kind of research with the methodological sophistication that the identification of a new syndrome would require.

The DoD and the DVA are sponsoring several large research studies that may provide more definitive answers as to whether there is a new, unique Persian Gulf Syndrome. An outline of the research studies that are relevant to the CCEP appears in a later section of this report.

Potential Relationship of Illnesses in CCEP Patients to Service in the Persian Gulf

As in previous conflicts, some CCEP patients may have developed illnesses that are directly related to their service in the Persian Gulf, such as (1) acute musculoskeletal injuries that were sustained during the war, (2) infectious diseases such as leishmaniasis that are very rare outside of the Middle East (Hyams et al., 1995), or (3) psychological stress experienced during or after the war that has caused or exacerbated physical or mental illnesses (Sutker et al., 1994a). Some CCEP patients also may have developed illnesses that are

coincidental with or predate, and that are therefore unrelated to, their service in the Persian Gulf. Physicians involved with the development and the administration of the CCEP have, in various public presentations, acknowledged that some CCEP patients have developed illnesses that are directly related to their service in the Persian Gulf. The recent DoD report on 10,020 CCEP participants, however, only touches on this issue indirectly (DoD, 1995d). The committee encourages the DoD to discuss the issue of causality explicitly and unambiguously in its future reports. Such a discussion might help to alleviate the current climate of confusion and mistrust that exists among some Persian Gulf veterans and the general public.

The time of onset of disease is closely related to the potential relationship of an illness and service in the Persian Gulf. The CCEP questionnaire includes an explicit question about the duration of symptoms in weeks; therefore, it would be possible to stratify the onset of each patient's symptoms relative to his or her service in the Persian Gulf. The recent DoD report on 10,020 participants, however, does not address the timing of exposures during Persian Gulf service in relation to the onset of symptoms (DoD, 1995d). The committee recommends that the DoD attempt to determine the timing of the onset of disease, especially for patients who have significant impairments. Review of military or civilian medical records that predate enrollment in the CCEP may provide contemporaneous documentation of the onset of symptoms in some patients, especially if the symptoms are serious. In addition, it is important to determine whether service in the Persian Gulf has contributed to the exacerbation of preexisting diseases in some CCEP patients.

Comparison of the CCEP Population with Other Populations

In its most recent report, the DoD compares the symptoms and diagnoses in the CCEP population with the symptoms and diagnoses in several community-based and clinically based populations (DoD, 1995d). For example, the DoD provides possible explanations for why certain diagnostic categories are more or less common in the CCEP than in the National Ambulatory Medical Care Survey. In the committee's view, interpretations based on comparisons with other populations should be made with great caution and only with the explicit recognition of the limitations of the CCEP as a self-selected case series. The CCEP was not designed to answer epidemiological questions, such as how the frequencies of certain diagnoses compare between the CCEP population and a control population. Instead, it was designed as a medical evaluation and treatment program. Indeed, the research aims of the CCEP do not appear to be stated explicitly, nor does there appear to be a concrete epidemiological study

plan. Without research hypotheses, it is not possible to judge whether any particular comparison group is appropriate.

Many different comparison groups are briefly mentioned in the DoD report on 10,020 CCEP participants (DoD, 1995d). Each individual population should be described to prevent confusion. Because of the self-selected nature of the CCEP population, a truly comparable reference group may not be available. For example, active-duty military personnel tend to be younger, predominately male, and healthy enough to work full-time. Since the physical requirements to join the military are relatively stringent, active-duty personnel are generally healthier than the average person in the same age group. In contrast, civilian patients who have been evaluated in primary care clinics may be older, may include more females, and may be too sick to work full-time. Because the CCEP population has concerns about chronic symptoms and is actively seeking health care, clinically based groups might be more appropriate for comparison than population-based groups.

The CCEP includes a wide variety of data gathered at many sites. Clinical evaluations were performed by different physicians in many locations and who possibly used a variety of diagnostic criteria. This is particularly true for diseases for which the diagnostic methods are not entirely routinize, such as neuropsychological disorders or sleep disorders. These data may not be appropriate for epidemiological purposes beyond the description of a case series because of the potential lack of uniformity in collecting the diagnostic information. For these reasons, it would be extremely difficult to establish causal relationships or to identify and characterize a new "Persian Gulf Syndrome" definitively by relying on data from the CCEP alone. The latitude permitted in the clinical examination program conflicts with the rigor necessary to answer an epidemiological question.

The CCEP data do have considerable clinical utility, and they could be used to address many important questions from a descriptive perspective. Many case series could be derived from these data, for example, a case series describing the sleep apneas identified in the CCEP population. In addition, the results of the clinical exams could provide guidance in the selection of research questions and in the design of future epidemiological research. In particular, certain hypotheses could be derived from the clinical exams, which in turn could lead to explicit choices in questionnaire design or laboratory tests. For example, the frequency of serious infectious diseases, such as leishmaniasis or malaria, is very low in the CCEP population; therefore, further epidemiological research should not focus solely on infectious diseases. The CCEP findings could be used to generate epidemiological questions on other types of diseases that are much more frequent in the CCEP population, such as musculoskeletal diseases. An outline of ongoing epidemiological research that is relevant to the CCEP is

provided in a later section of this report (see Epidemiological Research Relevant to the CCEP).

SPECIFIC MEDICAL DIAGNOSES

In addition to the committee's general review of symptoms and diagnoses, it has reviewed five disease categories in more detail. Three of these disease categories are the most prevalent in the CCEP population: psychiatric conditions; musculoskeletal conditions; and signs, symptoms, and ill-defined conditions. In addition, infectious diseases have been reviewed because of the possibility that troops deployed to the Persian Gulf may have acquired diseases that are unusual outside that region. Finally, the last category includes three conditions that have been reviewed because of their poorly defined nature: chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity.

Psychiatric Conditions

Three major issues that are relevant to psychiatric conditions will be discussed: (1) the prevalence and impact of psychiatric conditions among CCEP patients, (2) the standardization of psychiatric evaluations in the CCEP, and (3) the recognition of psychosocial stressors in the CCEP population, including relevant epidemiological research.

Prevalence and Impact of Psychiatric Conditions Among CCEP Patients

Of the primary diagnoses in the CCEP population, 19% are psychiatric conditions (DoD, 1995d). A primary or secondary diagnosis of a psychiatric condition has been made in 37% of CCEP patients. According to the DoD, the prevalence of psychiatric diagnoses in the CCEP population may be "somewhat higher than that found for other groups of health seeking individuals in which structured psychiatric interviews were used" (DoD, 1995d). The most common psychiatric conditions in the CCEP population are major and minor depression (diagnosed in 3% and 8% of all CCEP patients, respectively), PTSD (5%), adjustment disorder (4%), and mild anxiety syndromes (2%) (DoD, 1995d). In addition, personality disorders appear to be common in the CCEP populations; however, use of the section of the Structured Clinical Interview for DSM III-R (Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised) that is used to diagnose these disorders is not currently mandated by the DoD (Engel, 1995).

Many aspects of military service in wartime can cause significant physical and psychological stress. Physicians have observed that in many previous wars, including the Vietnam War, wartime stressors can lead to the development of higher rates of psychiatric illnesses than are observed in the general population. PTSD and major depression are prevalent problems in veterans. As might be expected from experiences in previous conflicts, many of the patients who have been evaluated in the CCEP have been diagnosed with psychological problems, as well as with other medical problems.

Patients need to understand that these are real diseases that cause real symptoms and that these diagnoses are made with objective criteria and are not merely "labels" that were applied because physical abnormalities were not found. The CCEP patients, as well as their primary care physicians, also need to understand the prevalence of and the concomitant morbidity that result from psychiatric disorders in the general population (major depression, for example). Finally, the CCEP patients need to be aware that effective treatments that actually ameliorate symptoms exist for many of these disorders.

In addition to the IOM committee on the CCEP, several other review groups have examined the health concerns of Persian Gulf veterans. Three major reviews have recognized the potential impact of psychological stress in this population, including rapid deployment, primitive living conditions in the desert, the threat of chemical and biological warfare agents, and actual combat exposure (Defense Science Board, 1994; NIH, 1994; IOM, 1995b).

The committee concludes that many of the psychiatric diseases in the CCEP population have both physical and psychological symptoms and manifestations. In its future reports, the DoD is encouraged to emphasize that psychosocial stressors can produce physical and psychological effects that are as real and potentially devastating as physical, chemical, or biological stressors. The DoD should also emphasize that thorough efforts to diagnose psychiatric conditions in the CCEP population may lead to appropriate, successful treatments.

The committee is particularly concerned about the CCEP patients who have developed or who are at risk of developing major depression or PTSD. These people need to be identified and provided with some form of preventive intervention. Some people can develop depression or PTSD as long as 5 years after a traumatic event, and they may also develop related delayed-onset problems such as substance abuse. In addition, there may be Persian Gulf veterans who currently have symptoms of depression or PTSD who have not sought medical care, and some form of outreach is needed to identify them and notify them that help is available through the CCEP. Some Persian Gulf veterans who have these conditions may be experiencing physical symptoms that could have psychological underpinnings. Both depression and PTSD could be underlying mechanisms for some sleep disorders, for example. There appears to be an unexpectedly high prevalence of sleep disorders in the CCEP

populations, which, in turn, could be contributing to other symptoms (Matthews, 1995).

Standardization of Psychiatric Evaluations in the CCEP

Psychiatric evaluations are mandated for all patients in Phase II of the CCEP. These include the Structured Clinical Interview for DSM III-R and the Clinician Administered PTSD Scale in addition to a clinical evaluation by a psychiatrist. With the use of such validated instruments, the psychiatric evaluations can be performed more systematically across the many hospitals in the country.

Nonetheless, there are difficulties in some patients in differentiating psychopathology versus illness behavior versus difficulties in adjustment to activities of daily living; that is, there is variability in the threshold of psychiatric diagnosis. This is complicated in patients who are strongly attached to a sickness role. As a result, there is likely to be variability in the CCEP psychiatric diagnoses despite strong efforts to standardize procedures. For instance, the proportion of patients who receive a primary diagnosis of a psychiatric disease varies considerably from site to site. For example, the rates of serious psychiatric diseases are particularly high at the Walter Reed Army Medical Center. In addition to the mandated tests, Walter Reed staff always include the Minnesota Multiphasic Personality Inventory and a social worker's evaluation in the psychiatric exam (Roy, 1995).

The committee recommends that the DoD consider methods of improving the standardization of the psychiatric evaluations in the CCEP. The DoD should consider establishing detailed guidelines for the psychiatric evaluations and should attempt to obtain greater standardization of these evaluations among the various hospitals across the country. These guidelines could provide suggested procedures for the use of selected self-report instruments for the assessment of the most commonly diagnosed disorders, as well as procedures for more indepth structured clinical interviews when indicated. Validated self-report instruments are available to assist primary care physicians in screening patients for common psychiatric conditions (Spitzer et al., 1995). It would be especially important to document the onset and course of symptoms and to investigate their possible link with psychosocial stressors associated with mobilization and return home, as well as with service-related exposures in the Persian Gulf region. This assessment would require an additional set of questions to supplement the questionnaire currently used in Phase I of the CCEP. The thorough assessment of psychosocial stressors is essential information for treatment planning for patients with complex, chronic symptoms.

Standardization of the neuropsychological evaluations is a related concern. The neuropsychological methods vary from pencil and paper testing at some

sites to computer-administered testing at other sites. This could lead to diagnostic variability from site to site. At some sites, it appears that patients receive only a computerized test battery without an individualized clinical evaluation. At these sites, it is unknown how cutoff scores for judging whether the patient's performance is abnormal were determined. It is also unknown how premorbid abilities are assessed. In addition, explicit criteria would be helpful for determining which patients would benefit from a neuropsychological evaluation. One method of achieving a better consensus, suggested by RMC physicians, is to convene a meeting attended by one psychiatrist and one neuropsychologist from each center to attempt to standardize their methods.

In addition to the standardization of psychiatric evaluations in the CCEP, the classification and coding of these diseases should also be standardized. In general, the ICD-9 coding of the diagnoses in the CCEP appears to be appropriate, but the categorization of some psychiatric and neurological conditions is confusing. Migraine and other severe headaches are categorized under the nervous system, tension headaches are categorized under psychological conditions, and still a third group of headaches is categorized under the group signs, symptoms and ill-defined conditions (DoD, 1995c). The classification of different types of headaches into these three separate categories may be consistent with ICD-9 coding rules, but the DoD should also report a special tabulation that combines all headaches into one group. This is particularly important, since 39% of the CCEP patients complain of headache symptoms (DoD, 1995d).

If psychiatric and neuropsychological diagnoses are made inconsistently or are not coded uniformly, the DoD will not be able to provide accurate and reliable summary data based on the combination of information from many patients. The DoD now has experience with more than 10,000 patients; therefore, the more frequent types of chart errors, omissions, or inconsistencies should be apparent by now. More explicit written instructions could be added to the CCEP guidelines to help prevent the most frequent problems found in the medical record-keeping and coding. These comments about inconsistencies are mainly aimed at the quality control necessary for accurate reporting of summary data rather than at the quality of the medical care itself.

Recognition of Psychosocial Stressors in the CCEP Population

A brief overview of the psychological stressors faced by the troops who were deployed to the Persian Gulf appears in two section in the DoD report on 10,020 CCEP patients: Potential Health Risks Associated with Persian Gulf Deployment, and Individual and Group Response to Environmental Hazards as a Factor Contributing to Health Consequences Among CCEP Participants (DoD, 1995d). In future reports, the DoD should consider expanding this description

to provide a more thorough, in-depth discussion of the psychological stressors that were present during the Persian Gulf War. For example, although there were few American casualties, thousands of Iraqi soldiers were killed. Witnessing large numbers of dead Iraqi soldiers or involvement in their burial has been associated with the development of significant psychological distress (Sutker et al., 1994a,b).

The DoD and the DVA have recognized the need for epidemiological research on the psychological stressors of the Gulf War and on the prevalence of psychiatric outcomes among Persian Gulf veterans. This need was summarized in a recent document that outlines their current research strategy (PGVCB, 1995a). The justification by the DoD and the DVA for this type of research is as follows (PGVCB, 1995a):

Psychiatric morbidity among U.S. troops deployed to the Persian Gulf area was predicted even though the war was of short duration, resulted in a relatively low number of casualties, and positive support for the war prevailed at home. Persian Gulf veterans were exposed to many psychophysiological stressors besides direct combat, such as sudden mobilization for military service (especially among members of reserve and National Guard units), exposure to dramatic oil well fires, the constant threat of chemical and biological warfare agents, and fear of combat in general. A wide range of somatic and psychological responses could be expected from individuals deployed to the Persian Gulf area from stress associated with deployment (Wolfe et al., 1993). . . .

A variety of symptoms have been reported by Persian Gulf veterans. Some symptoms may be related to post-traumatic stress disorder (PTSD). Published findings (Sutker et al., 1993; Sutker et al., 1994a,b; and Wolfe et al., 1993) suggest an increased prevalence of PTSD and other psychiatric diagnoses, such as depression, in some Persian Gulf War veterans. Although the prevalence of these disorders was found to be lower than that found among Vietnam veterans, it is evident that stressors during the Persian Gulf conflict were sufficient to cause significant psychiatric morbidity. Because of the low level of combat experienced by many troops in the Persian Gulf conflict, the presence of psychiatric problems among some returnees suggests the importance of stress other than actual combat as a precipitating factor.

Currently, the DoD and the DVA are funding several research projects relevant to psychiatric conditions in Persian Gulf veterans (PGVCB, 1995a). These include four DoD and six DVA projects, which will acquire self-reported data on exposures to psychophysiological stressors among Persian Gulf veterans. These projects will also collect questionnaire data, which will allow the

development of prevalence estimates of psychological symptoms and diagnoses (PGVCB, 1995a).

It is possible that the DoD will be able to use the results of these epidemiologic studies on psychiatric conditions to revise the CCEP, that is, to revise the standardized questionnaires or to add or delete targeted lab tests or specialty consultations. In addition, the CCEP clinicians may be able to utilize these results in the counseling and treatment of their patients. These results may also be useful for the DoD in its planning to minimize the effects of psychosocial stressors in future deployments through the use of preventive medicine interventions. For instance, a better understanding of the psychological symptoms in the CCEP, coupled with more information on the deployment circumstances associated with patients with these problems, might suggest hypotheses for further research on prospective interventions.

Musculoskeletal Conditions

Musculoskeletal conditions account for 17% of the primary diagnoses in the CCEP population. A primary or secondary diagnosis of a musculoskeletal condition has been made in 45% of the CCEP patients. Of these conditions, 51% are included in three categories: joint pain, osteoarthritis, and backache/lumbago (DoD, 1995d).

These musculoskeletal conditions could be related to the physical demands of military service. Occupational and recreational overuse injuries frequently occur as a consequence of the physical activities associated with military training and operations (DoD, 1995d). It is fortunate that most of these musculoskeletal conditions do not appear to cause serious impairment. Of the patients who had a musculoskeletal condition as their primary diagnosis, 82% stated that in the previous 90 days they had not missed even 1 day of work because of illness (DoD, 1995c).

The draft and final DoD reports on 10,020 CCEP patients do not provide adequate details for the IOM committee to make a thorough evaluation of the diagnostic categorization of musculoskeletal conditions (DoD, 1995c,d). All three of the categories of musculoskeletal conditions mentioned—joint pain, osteoarthritis, and backache/lumbago—are broad and vague; therefore, some explicit examples of the actual diseases categorized under musculoskeletal conditions would be helpful. More explanation about the diagnostic aspects of these musculoskeletal conditions would be useful, for example, information on single-joint involvement versus multijoint conditions or articular versus non-articular conditions. In addition, details on disease severity and disease activity would be useful.

The DoD and DVA apparently are not currently performing any epidemiological investigations that are focused on musculoskeletal conditions among Persian Gulf veterans (PGVCB, 1995a). The DoD and DVA are performing several general health surveys among Persian Gulf veterans in which musculoskeletal conditions may be a minor consideration. The IOM committee believes that the DoD and the DVA should consider placing more emphasis on research on musculoskeletal conditions, since these are the most prevalent disorders among the CCEP populations. A variety of instruments are available for use in epidemiological research on musculoskeletal conditions. Musculoskeletal conditions represent a significant cause of morbidity among military personnel in general, that could be prevented if risk factors could be identified (DoD, 1995d).

Signs, Symptoms, and Ill-Defined Conditions

The ICD-9 category of signs, symptoms, and ill-defined conditions (SSIDC) is extremely heterogeneous. It encompasses generalized symptoms such as fatigue and malaise, nonspecific abnormal laboratory results (i.e., an elevated sedimentation rate), and signs and symptoms that prove to be transient (i.e., a history of a skin rash). In general, no significant objective anatomical, pathological, or biochemical abnormalities are detectable in this category. Since many specific conditions that are not otherwise classified in ICD-9 are categorized as SSIDC, coding a diagnosis as SSIDC may reflect limitations in the ICD-9 criteria, as much as a physician's inability to explain the condition.

SSIDC is the primary diagnosis for 17% of CCEP patients, and 41% of CCEP patients have a primary diagnosis or a secondary diagnosis of SSIDC (DoD, 1995d). This group does not have homogeneous symptoms, and some of the patients in this group have well-recognized diseases, such as dyslexia or sleep apnea, which are not classified elsewhere in ICD-9. Therefore, it should not be concluded that the 17% of the CCEP patients whose primary diagnosis is SSIDC have a "mystery illness." Rather, the committee recommends that in future reports the DoD attempt to clarify the types of disorders that are included in the category of SSIDC. Individuals with these signs, symptoms, and ill-defined conditions should be evaluated in a rigorous manner, just as individuals with any other symptoms are evaluated.

Infectious Diseases

An overview of the infectious diseases that occurred during the Persian Gulf War was recently published (Hyams et al., 1995). The most frequently reported

infectious causes of acute morbidity were generally mild cases of acute diarrhea and upper respiratory infections, neither of which would be likely to lead to long-term sequelae. There were unexpectedly low rates of arthropod-borne infections, for example, sandfly fever. These very low rates were due to low insect populations in the winter months. A total of 226 noncombat deaths, primarily from accidental injuries, were reported during the Persian Gulf War. No deaths due to infectious diseases were reported (Helmkamp, 1994; Hyams et al., 1995).

The DoD report on 10,020 CCEP patients summarized the types and prevalence of infectious diseases as follows (DoD, 1995d):

The threat to deployed military personnel posed by infectious diseases was recognized and preparations were made from the earliest stages of Operation Desert Shield. Specific infectious diseases observed in U.S. troops during Operations Desert Shield/Storm conformed with expected disease threats. Data suggest that overall exposure to recognized pathogens was quite low. Furthermore, it suggests that no route of infection, other than ingestion of locally-produced food, was common. The reported incidence of infectious diseases observed during the Operations is relevant to evaluation of current health complaints of Gulf War veterans. . . .

The low incidence of leishmaniasis during and immediately after Operations Desert Shield/Storm, the absence of other sandfly-borne diseases in our troops, and the low prevalence of objective findings pointing to leishmania disease among 10,000 CCEP patients, all indicate that viscerotropic leishmaniasis plays no significant role in the current complaints of Gulf War veterans.

The CCEP itself has identified a wide variety of infectious diagnoses. Of these, by far the largest group has been fungal infections of the skin due to fungi common in the United States. Virtually all of the remaining infections have represented common illnesses, such as sinusitis, diarrheas, and a few cases of viral hepatitis, not specific to the Persian Gulf region. The overwhelming majority of these diagnoses represent incidental diagnoses which would not explain persistent systemic complaints.

The IOM committee concludes that infectious diseases are not a frequent cause of serious illness in the CCEP population. Only 3% of the CCEP population has a primary diagnosis of an infectious disease. A primary or secondary diagnosis of an infectious disease has been made in 9% of the CCEP population (DoD, 1995d). Of the 278 patients who have a primary diagnosis of

an infectious disease, 81% stated that in the previous 90 days they had not missed even one day of work because of illness (DoD, 1995c).

A variety of organ systems have been affected by infectious diseases in the CCEP population, without any observable patterns. The majority of these diseases have been minor or asymptomatic, or they were diseases that were diagnosed before the patient enrolled in CCEP (Gasser, 1995). To date, very few CCEP patients have demonstrated the classical objective physical and laboratory abnormalities that would indicate a chronic infectious process, such as documented fever, leukocytosis, lymphadenopathy, hepatomegaly, or splenomegaly (Gasser, 1995; Hyams et al., 1995; PGVCB, 1995b).

The IOM committee concludes that on the basis of the current evidence, it is unlikely that a significant proportion of Persian Gulf veterans are afflicted with some previously unknown pathogen that is evading the current diagnostic efforts.

Chronic Fatigue Syndrome, Fibromyalgia, and Multiple Chemical Sensitivity

The IOM committee's review of the CCEP protocol suggests that data on chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivity (MCS) may have been collected by various diagnostic methods. For this reason, it is not possible to estimate the prevalence of these conditions from the CCEP data.

In the clinical evaluations, the IOM committee believes that data should be collected by using established diagnostic criteria for CFS and FM. A widely accepted set of diagnostic criteria does not exist for MCS. Consequently, the medical evaluation in CCEP cannot be expected to diagnose the clinical syndrome of MCS. If more is to be learned about the relationship between these disorders (CFS, FM, and MCS) and Persian Gulf service, they should be included among the epidemiological research studies that are ongoing or planned for the future.

The symptoms of some of the CCEP patients are similar to or overlap the nonspecific symptoms that previous authors (Holmes et al., 1988; Wolfe et al., 1990) have described for CFS or FM, as shown in Table 7 of the DoD report on 10,020 patients (DoD, 1995d). These nonspecific symptoms include fatigue, joint and muscle pain, headache, sleep disturbance, and depressed mood. Because of the thorough, systematic workup mandated in the CCEP, many disorders that could contribute to sleep disturbance and fatigue have been diagnosed. These have included obstructive sleep apnea, gastroesophageal reflux, hyperthyroidism, chronic sinusitis, and PTSD. For example, 5% of the first 10,020 CCEP patients were diagnosed with PTSD (DoD, 1995d). These

diligent efforts to unmask occult medical problems that could substantially contribute to fatigue have been productive and should continue.

USE OF THE CCEP RESULTS FOR EDUCATION, IMPROVEMENTS IN THE MEDICAL PROTOCOL, AND OUTCOME EVALUATIONS

The results of the CCEP can be used for several purposes, including to educate Persian Gulf veterans and the physicians caring for them, to improve the medical protocol itself, and to evaluate patient outcomes. In addition, the early progress of SCC should be evaluated so that its successful elements can be disseminated to other hospitals involved in the CCEP.

Use of the CCEP Results for Education

The results of the CCEP should provide valuable information to Persian Gulf veterans and the physicians who are caring for them. The IOM committee encourages the DoD to continue to release its analysis of the results of the CCEP on an ongoing, periodic basis. Several audiences that would be interested in these results include active-duty members of the service, veterans, members of the U.S. Congress, the lay media, as well as military, DVA, and civilian medical and public health professionals.

The medical findings of the CCEP should be distributed promptly to all primary care physicians at the MTFs and RMCs. This would provide feedback on their diagnostic decision-making. Information on the frequencies of particular symptoms and their specific diagnoses made in the CCEP population could be useful, for instance, in developing a differential diagnosis for individual patients. The CCEP medical findings would also be of interest to physicians in the DVA system and in the general community. Almost 500,000 of the 700,000 Persian Gulf veterans had been discharged from active duty as of mid-1995; therefore, they are currently seeking health care from DVA or from community-based physicians, rather than from the DoD.

A more concise version of the DoD report on 10,020 patients, written in nontechnical language and with clearly stated conclusions, should be developed for a target audience of active-duty service personnel and veterans. These individuals have the greatest need to understand the results of the CCEP and how to interpret them. Currently, many active-duty military personnel and veterans seem to receive much of their information about the CCEP through the lay media. If the DoD developed and distributed a fact sheet or newsletter aimed at Persian Gulf veterans, the information on the CCEP would be more accurate and more comprehensive than most reports in the general news media. This would also provide an additional opportunity to notify the readers about the

availability of the medical exam in the CCEP, the hotline number, and the eligibility criteria.

The DoD should also consider developing for clinical use in the CCEP a more comprehensive document that describes the many potential exposures in more detail. Patients frequently ask their physicians about what they were exposed to, and if the CCEP physicians could obtain a clearer picture of the possible range of exposures, they might be able to counsel their patients more effectively. Any document that is prepared, however, must make clear what is known and what is unknown about the relationship between these stressors and the physical or psychological consequences. The DoD report on 10,020 CCEP patients and several other recent reports have also outlined the potential physical, chemical, biological, and psychological stressors in the Persian Gulf War (Defense Science Board, 1994; NIH, 1994; IOM, 1995b; DoD, 1995d; PGVCB, 1995a,b). Even though these reports overlap, most are not comprehensive or designed for clinical use.

Use of the CCEP Results to Improve the Medical Protocol

The DoD now has results on the examinations of more than 10,000 CCEP patients. These results could be used to improve the standardized questionnaires, lab tests, and specialty consultations. Three examples are provided here, but other beneficial revisions to the protocol are certainly possible.

Some data on potential psychological stressors of the war are available (Sutker et al., 1993, 1994a,b; Wolfe et al., 1993). More refined questions related to these stressors could be added systematically to the Phase I medical history. The CCEP physicians might find this information useful in diagnosing and counseling their patients. In addition, it may be possible to identify patients who are at increased risk of psychological problems on the basis of their experiences in the war. For example, it has already been recognized that direct combat exposure is a risk factor for developing a psychiatric disease. In addition, recent studies have demonstrated that exposure to death—that is, viewing or having to bury dead Iraqi soldiers—is also a risk factor (Sutker et al., 1994a,b). Perhaps explicit questions on death exposure and other known risk factors could be added to the Phase I questionnaire.

The CCEP results should be analyzed to determine whether there are lab tests or specialty consultations that should be added systematically to Phase I to increase its diagnostic yield. Among the first 10,020 CCEP patients, about 8,300 completed their evaluations in Phase I and about 1,700 completed their evaluations in Phase II (DoD, 1995d). Diseases that are diagnosed relatively

frequently in Phase II may often be overlooked in Phase I. If such diseases could be identified, perhaps appropriate screening instruments could be added to Phase I. A hypothetical example is depression, which has been diagnosed in 11% of the 10,020 patients (DoD, 1995d). If the recognition of this disease has occurred predominantly during Phase II, then perhaps a screening questionnaire for it could be added systematically in Phase I for use by primary care physicians.

The DVA uses a protocol similar to that used in the CCEP called the Uniform Case Assessment Protocol (UCAP). The methods and clinical results of the CCEP and UCAP should be compared to coordinate and improve the two programs.

Use of the CCEP Results for Patient Outcome Evaluations

On the basis of more than 10,000 patient evaluations to date, RMC physicians could begin to perform a series of targeted patient evaluations. The most common diseases in the CCEP could be identified, and suggested approaches to patient treatment could be developed. Consensus guidelines for the treatment and counseling of CCEP patients who have the most common disorders could be useful for primary care physicians. Depression is a common disease that most CCEP physicians are likely to encounter.

If one RMC has had a lot of experience with a particular disease category and some measure of success in its treatment, the DoD could ensure that a description of their successful methods is communicated to the other MTFs and RMCs across the country. For example, Walter Reed Army Medical Center had performed more than 500 Phase II evaluations by mid-1995, all of which included psychiatric evaluations (Roy, 1995). Walter Reed physicians have diagnosed debilitating psychiatric diseases in a high proportion of these patients. If Walter Reed staff have identified the elements of a psychiatric treatment program that are particularly effective or ineffective in a military population, a summary of these elements could be shared among the CCEP physicians nationwide.

Another potential candidate for outcome evaluation could be an investigation of the types of CCEP patients who apply for a medical discharge from the military. The DoD could perform a review of the types and severities of the disorders among CCEP patients who have applied for disability payments or for medical discharge from the service. In addition, the final disposition of these cases could be evaluated, including the potential relationship between particular diseases and Persian Gulf service. The DoD could use the results of these disability determinations to predict which diseases are likely to be associated with the most impairment among CCEP patients in the future. The DoD could

also use these results to develop rehabilitation and early intervention methods for impaired Persian Gulf veterans, such as the SCC, which is described below. Another reason to analyze these disability claims would be to investigate possible preexisting risk factors for the development of the impairment. If such risk factors are identifiable, then targeted preventive medicine interventions could be planned for individuals participating in future overseas deployments.

Specialized Care Center

Overview of the Goals, Structure, and Early Progress of the SCC

On June 9, 1995, the IOM committee made a site visit to the SSC at the Walter Reed Army Medical Center. Presentations were given by three of the SCC staff who have developed and implemented the program. In addition, the committee interviewed 4 of the first 10 patients who graduated from the SCC. This brief description of the SCC and the committee's comments on the program arise primarily from information gathered at the site visit.

The SCC was developed in response to a need for "further treatment and diagnosis for conditions possibly related to environmental and/or psychosocial stressors associated with deployment" (Roy, 1995). Pain treatment centers were used as the model for development of the SCC. The first group of six patients entered the SCC system on March 22, 1995. The three major SCC referral criteria are (1) symptoms without a clear diagnosis; (2) symptoms out of proportion to the diagnosis; or (3) a diagnosis of somatoform disorder, chronic fatigue syndrome, multiple chemical sensitivity, fibromyalgia, or PTSD. In addition, the patients should be unable to meet weight or fitness standards or show other signs of significant impairment.

The SCC is a very structured 3-week inpatient program that incorporates rigorous physical training and intensive mental health components. The main goals of the SCC are to refocus individual patients from illness to wellness and to return participants to full duty within 6 months. The SCC participants are required to sign a contract stating that they will participate 100% in all activities and refrain from interference in the efforts of other patients or they will be subject to termination from the program. A follow-up visit after 6 months is planned for each graduate at Walter Reed.

The first 15 SCC patients were all enlisted men, with a mean age of 35 years (range of 24-58 years) (Roy, 1995). All of the first 15 SCC patients reported 10 or more somatic symptoms at entry.

The SCC program does have several limitations, including a low referral rate by CCEP physicians, a low enrollment rate, and uncertainty about the availability of follow-up care, which may result in regression (Roy, 1995). For

the first 2 months of the SCC, 50% of the referred patients declined enrollment. If a candidate for the SCC was in the reserves, it was difficult to leave a civilian job for 3 weeks or longer. Some active-duty personnel declined participation because they had already gone through the disability process and they were separating from the service.

The SCC staff are concerned about the effect that lack of follow-up will have on any progress made during the SCC program. Many MTFs have only one psychiatrist and one social worker, and these personnel already have very heavy workloads (Follansbee, 1995). At the time of discharge from Walter Reed, there is an effort to link the patient to a physician, chaplain, or social worker who can provide follow-up care at the local MTF.

Four of the first 10 SCC graduates were briefly interviewed by the IOM committee. All four stated they were very satisfied with the care that they had received in the SCC. All reported greatly improved health and outlook on life. These four SCC patients did express concern about the accessibility of high-quality follow-up care. They stated that if they developed a sudden worsening of symptoms, they would want to return to Walter Reed for treatment, even though they all lived at least several hundred miles away. They were concerned that they could not expect to receive timely, high-quality medical care from an empathetic physician at an MTF.

Committee Comments on the Goals, Structure, and Early Progress of the SSC

The IOM committee concludes that the DoD has made serious efforts to develop an SCC program that has ambitious goals for a select group of seriously impaired military personnel. The committee's review should be considered preliminary, however, because it is based on one visit and it is still early in the development of the program.

The SCC currently performs a thorough reevaluation of each patient's medical problems. SCC physicians should consider limiting the diagnostic role that they play to focusing on the incoming patients who have been very difficult to diagnose at the RMC level. Instead, the SCC should focus on providing multidisciplinary treatment modalities that are not readily available at the RMC level.

The need for individualized follow-up is crucial for the types of difficult patients who are likely to be treated at the SCC. Medical staff at the SCC will need to know whether a particular therapeutic plan is feasible at the patient's nearest MTF and whether long-term follow-up care can be performed. The primary care physician at the MTF needs to encourage continuous patient compliance with the carefully designed, individualized therapeutic regimens.

This could be particularly difficult with patients who have somatoform disorders, substance abuse problems, and other debilitating psychiatric problems.

A 6-month follow-up evaluation at Walter Reed is planned for each SCC patient. The SCC physicians should develop a set of relatively objective measures of functional status for this evaluation. These could include (1) appropriate utilization of medical care, (2) appropriate use of medications or other methods to cope with symptoms, (3) general level of activities of daily living, (4) employment status, and (5) status of interpersonal relationships.

The overall SCC program itself needs an evaluation component after several of its graduates have returned for their 6-month reevaluations. Several issues will need to be evaluated in light of the successes and barriers that the program has experienced. These include eligibility criteria for patients; roles of the SCC in a diagnostic reevaluation of patients; successful continuity of care of patients, with shared responsibility by the SCC and MTFs; and the unique need for the SCC, beyond the usual standard of a tertiary care medical center.

The committee believes that the DoD has taken a serious approach to the treatment and rehabilitation of these impaired patients who have treatable, chronic diseases. Because this program is very labor intensive, it is probably very expensive on a per-patient basis. At the same time, the potential benefits for each patient could be high, if successful rehabilitation of serious, long-term impairment can be achieved. Subsequent evaluations of the SCC program should investigate its costs and benefits, if possible.

If the SCC program is successful in improving the health and functional status of its patients, perhaps the elements that are most effective in enabling the patients to cope with their symptoms could be identified. Perhaps some of these elements could be disseminated and integrated into existing MTF programs that are close to where CCEP patients live and work. If soldiers could participate in some type of therapeutic program, in combination with their regular jobs, more individuals could participate. Some of the interventions that are part of the SCC could probably be implemented by social workers, nurses, or chaplains at the MTF level.

EPIDEMIOLOGIC RESEARCH RELEVANT TO THE CCEP

The DoD and DVA are performing or funding several epidemiologic studies that may have implications for CCEP patients and their physicians. These include (1) studies focusing on exposure assessment and (2) studies focusing on health conditions among Persian Gulf veterans. The results of these studies may be useful for making revisions or improvements in the CCEP medical protocol itself, for example, to revise the standardized questionnaires or to add or delete targeted lab tests. The study results may also be useful in the counseling and

treatment of CCEP patients. Data from individuals in the CCEP are also being used in some of these epidemiological studies. In these studies, the serious limitations of the CCEP data for epidemiological purposes that were previously identified must be kept in mind.

Exposure Assessment Research Relevant to the CCEP

Military personnel serving in the Persian Gulf were potentially exposed to a large number of physical, chemical, biological, and psychological stressors. The DoD and DVA are performing or funding research on a variety of these potential stressors. The CCEP population is serving as the study group for one of these projects. Several different groups of Persian Gulf veterans are being studied in the other projects (PGVCB, 1995a).

The most important exposure assessment research involves the development of a geographical information system, which will contain data on the locations of military units on a daily basis during the Persian Gulf conflict. Unit diaries, where a unit consists of about 100 troops, were maintained on a daily basis for all units (PGVCB, 1995a). Information on location down to the individual service member was not recorded, but matches between units and individuals can be made. The computerization of all unit locations, as a function of time, is expected to be complete sometime in 1996 (PGVCB, 1995a). This database will be a valuable asset to many of the health studies.

The DoD is currently analyzing potential exposures among the CCEP population using unit of assignment codes (UICs). So far, there does not appear to be a clustering of CCEP patients in particular UICs (DoD, 1995d). The IOM committee encourages DoD to perform further investigations on the war and postwar experiences of individuals in the UICs with higher rates of CCEP participation. In addition, the committee encourages the DoD to investigate exposures that were restricted to particular locations or special occupational groups, such as troops who had direct combat exposure. The types of symptoms and diseases in CCEP participants in these special groups and UICs could be analyzed and contrasted with the symptoms and diagnoses of CCEP participants in other units. One unavoidable drawback to the UIC approach to exposure assessment, however, is that some of these units include as many as thousands of service personnel. Because of this, the potential exposure to a particular stressor, for which an entire unit may have been at risk, may not be applicable to a particular individual.

Health Outcome Research Relevant to the CCEP

Three general types of health research questions are relevant to the CCEP population. First, how does the prevalence of symptoms and diseases, in general, compare between Persian Gulf veterans and an appropriate control population? Second, how does the prevalence of certain disease categories compare between Persian Gulf veterans and an appropriate control population? Here, there are at least three major disease categories that may merit research attention: (1) psychiatric diseases and (2) musculoskeletal conditions, because they are the most prevalent disease categories in the CCEP population, and (3) poorly defined conditions, such as chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity. The third major research question is whether there is clinical or epidemiological evidence for a new, unique Persian Gulf Syndrome. Research relevant to the existence of a possible new syndrome has been discussed in detail previously.

Several ongoing and planned research projects will compare the prevalence of symptoms and diseases reported by Persian Gulf veterans with the prevalence reported by control groups of nondeployed veterans (PGVCB, 1995a). Most of these studies will acquire data on self-reported general or nonspecific symptoms, such as fatigue, headache, and memory loss. Two of these studies include physical examinations to validate self-reported symptoms in a subset of the study groups (PGVCB, 1995a). None of these studies appears to emphasize musculoskeletal conditions.

Psychiatric symptoms, such as depression, and neuropsychological symptoms, such as memory loss, are very common in the CCEP population. Several DoD, DVA, and U.S. Department of Health and Human Services (DHHS) research projects are focused on these symptoms and on corresponding diseases. These research projects were described earlier in some detail in the section Psychiatric Conditions.

Several DVA and DHHS projects are investigating the prevalence of poorly defined symptom complexes, such as chronic fatigue syndrome, fibromyalgia, or multiple chemical sensitivity (PGVCB, 1995a). The prevalence of self-reported symptoms relevant to these three conditions will be compared between veterans deployed to the Persian Gulf and veterans deployed elsewhere.

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Appendix A

Agendas for the Four Meetings of the IOM Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

EVALUATION OF THE U.S. DEPARTMENT OF DEFENSE PERSIAN GULF COMPREHENSIVE CLINICAL EVALUATION PROGRAM

Institute of Medicine Meeting of the Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

Foundry Building, Room 2003 Washington, D.C.

October 24, 1995

AGENDA

9:00 a.m. Executive Session

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Orientation and introduction
Bias and conflict of interest discussion
Planning for the day's activities

9:30 a.m. DoD Presentations

Background and overview Dr

Drs. Bailey and Martin

(10 min)

Descriptive statistics and findings

Dr. Erdtmann

(25 min)

Regional summaries

Six clinicians

(90 min)

Overall findings regarding

Dr. Anders

Dr. Murphy

unexplained illnesses

(20 min)

11:55 a.m. U.S. Department of Veterans

v etel alls

Affairs

12:00 p.m. Working Lunch-Discussion of Preliminary Findings

2:00 p.m. Discussion of Plans for the CCEP and IOM Activities

3:00 p.m. Executive Session

5:00 p.m. Adjourn

Institute of Medicine

Meeting of the Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

Foundry Building, Room 2004 Washington, D.C.

March 10, 1995

AGENDA

8:00 a.m. Breakfast

8:30 a.m. Executive Session

Orientation and introduction

Bias and conflict of interest discussion

Discussion of charge to the CCEP committee

Overview of the charge to the MFUA Persian Gulf Committee—Dr. Mundt

10:00 a.m. DoD Presentations

Background and overview of the CCEP

Dr. Bailey

(10 min)

Clinical approach to CCEP patients

Dr. Matthews

(20 min)

CCEP descriptive statistics and findings

(includes spouses and children)

Dr.O'Donnell

(20 min)

Infectious diseases in the CCEP

Dr. Gasser

(20 min)

Chronic fatigue syndrome/fibromyalgia/

multiple chemical sensitivity

Dr. Cooper (20 min)

EVALUATION OF THE U.S. DEPARTMENT OF DEFENSE PERSIAN GULF COMPREHENSIVE CLINICAL EVALUATION PROGRAM

Sleep disorders

Dr. Matthews (15 min)

11:45 a.m. Break

40

12:00 a.m. Working Lunch and Continuation of DoD Presentations

Psychiatric diagnoses Dr. Follansbe

(15 min)

Stress—related disorders in Persian Gulf
veterans

Drs. Lindquist
and Malone

(15 min)

Description of ill-defined conditions Dr. Anders (includes stratified analysis of "other (20 min)

conditions")

Typical medical symptoms seen in a Dr. Kroenke military ambulatory care setting (20 min)

Overview of potential Persian Gulf war exposures: physical, chemical, biological (30 min)

Specialized Care Centers—concept and Drs. Bailey and

operations Blanck (20 min)

DoD closing remarks

Dr. Joseph
(10 min)

2:15 a.m. General Discussion and Questions

Executive Session

and psychological

5:00 a.m. Adjourn

3:00 a.m.

8:00 a.m.

Institute of Medicine

Meeting of the Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

June 8-9, 1995

Foundry Building, Room 2004 Washington D.C

June 8, 1995

AGENDA

Continental Breakfast

8:30 a.m.	Executive Session		
9:30 a.m.	DoD Presentations		
	Introductory Remarks	Dr. Mazzuchi	
	Overview of CCEP descriptive statistics and findings (includes spouses and children)	Dr. O'Donnell (60 min)	
	Psychological conditions in the CCEP	Dr. Engel (15 min)	
	Musculoskeletal conditions in the CCEP	Dr. Vogelgesang (15 min)	
	Digestive conditions in the CCEP	Dr. Cheney (15 min)	
	Nervous conditions in the CCEP	Dr. Dutka (15 min)	
	Respiratory conditions in the CCEP	Dr. Anders (15 min)	

EVALUATION OF THE U.S. DEPARTMENT OF DEFENSE PERSIAN GULF COMPREHENSIVE CLINICAL EVALUATION PROGRAM

Description of Ill-defined Conditions (including stratified analysis of "other conditions")

Dr. Anders (20 min)

12:05 p.m. Lunch in Conference Room

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12:30 a.m. Overview of the Department of Dr. Veterans' Affairs Persian Gulf Registry (30)

Dr. Murphy (30 min)

1:00 p.m. DOD Presentations, Continued

Chronic fatigue syndrome in the CCEP

Dr. Cooper (20 min)

Sleep disorders in the CCEP

Dr. Matthews (10 min)

Neurocognitive impairment in the CCEP

Dr. Matthews (10 min)

Spectrum of disability among CCEP

patients

Dr. Trump (10 min)

Patient treatment and follow-up at MTF and RMC levels (including results of patient satisfaction questionnaires)

Dr. Trump (20 min)

Discussion and interpretation of the

results of the CCEP

Dr. Kroenke (40 min)

3:10 p.m. General Discussion and Questions

3:40 p.m. DoD Closing Remarks

Dr. Joseph (20 min)

4:00 p.m. Executive Session

6:00 p.m. Adjourn

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Walter Reed Army Medical Center

June 9, 1995

AGENDA

8:30 a.m. Presentation by CCEP physicians about the Specialized Care Centers - including purposes, procedures, logistics, successes and limitations, to date

10:00 a.m. IOM Committee Meeting With Small Group of CCEP Patients

11:30 a.m. Executive Session

12:30 p.m. Adjourn

Institute of Medicine

Meeting of the Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

National Academy of Sciences, Room 150 Washington, D.C.

September 6, 1995

AGENDA

9:00 a.m. Continental Breakfast

9:30 a.m. General Discussion of Draft Final Report

Committee assessment of the overall goals and procedures

of the CCEP

Implementation of the CCEP

10:30 a.m. Discussion of the Analysis and Interpretation of the Results

of the CCEP

Comparison of the CCEP population with other populations Committee comments on the symptoms and diagnoses in the

CCEP population

Potential relationships of illness in CCEP patients to

Persian Gulf service

Clinical evidence for a new, unique Persian Gulf syndrome

11:30 a.m. Discussion of the Committee Comments on Specific Medical

Diagnoses

Psychological conditions Musculoskeletal conditions

Signs, symptoms, and ill-defined conditions

Infectious diseases

12:00 p.m. Lunch in Conference Room

12:30 p.m. Discussion on Chronic Fatigue Syndrome, Fibromyalgia,

and Multiple Chemical Sensitivity

1:30 p.m. Discussion on the Potential Preventive Medicine Lessons

from the Persian Gulf War and the CCEP

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2:30 p.m. Discussion of the Potential Topics for the DoD and the IOM to Consider in Year 2 of the CCEP

3:30 p.m. Discussion of Additional Conclusions and Recommendations to be Included in the IOM Final Report on the CCEP

5:00 p.m. Adjourn

Appendix B

Outline of the Standardized Medical Protocol:
Selected Pages from the
Comprehensive Clinical Evaluation (CCEP) Guide,
January 5, 1995, U.S. Department of Defense

FORM REQUIREMENTS

At the MTF level, the CCEP record should include all CCEP forms and relevant medical data to the program.

Blank forms included with this guide supersede previous editions of these forms and are intended to be used with the new CCEP.

All individual forms will be complete and legible.

Forms forwarded to NMIMC and maintained in the participant record shall be in the following order:

Phase I completed:

MTF Phase I Diagnosis Form
Patient Questionnaire
Provider-Administered Symptom Questionnaire
Information Release Form
Declination/Completion Form

Phase II completed:

RMC Phase II Diagnosis Form Declination/Completion Form

MEDICAL PROTOCOLS

The CCEP is based upon a thorough clinical evaluation which emphasizes comprehensive and continuous primary care. The local MTF primary care provider maintains responsibility for patient evaluation and care throughout the CCEP process.

Medical Treatment Facility (Phase I)

Phase I will consist of a comprehensive history and medical evaluation with completion of Phase I questionnaires and related forms. The examination, both in content and quality, should parallel an in-patient admission work-up. The Phase I examination will include a complete medical history including: family, occupation, social (including tobacco, alcohol and drug use), exposure to possible toxic agents, psychosocial condition and review of

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symptoms. The provider will specifically inquire about the symptoms listed on the CCEP Provider-Administered Patient Questionnaire. A comprehensive medical evaluation, with focused attention to the patients symptoms and health concerns, should be conducted.

Individuals who, after completing MTF Phase I evaluations do not have a clearly defined diagnosis which explains their symptoms should be reviewed by the CCEP designated physician for further evaluation and consultations needed and/or for referral to the RMC.

Phase II Level Evaluations are performed only after complete clinically indicated evaluations (including appropriate specialty consultations) are conducted at the MTF and the RMC.

Phase I Laboratory Tests

CBC U/A SMA-12

Regional Medical Center (Phase II)

Phase II evaluations consist of the following laboratory tests, consultations and as necessary, symptom-specific examinations. Elements of the Phase II evaluation may be accomplished by the local MTF as needed in the comprehensive evaluation of the Phase I patient in order to obtain a definitive diagnosis.

Phase II Laboratory Tests

CBC

Hepatitis Serology

Sedimentation Rate (ESR)

HIV testing

C-Reactive Protein

VDRL

Rheumatoid Factor

B12 & Folate

ANA

Thyroid Function Tests

Liver Function

CPK

Urinalysis

TB skin Test (PPD) with controls

Chest X-ray

Phase II Consults

(if not accomplished at MTF level)

Dental: Dental only if participant's annual screening not done.

Infectious Disease

Psychiatry: With Physician Administered Instruments:

Structured Clinical Interview for DSMIII-R (SCID) (delete modules for mania and psychosis) Clinician Administered PTSD Scale (CAPS)

Neuropsychological Testing: Only as indicated by psychiatry consult

SYMPTOM SPECIFIC EXAMINATIONS

The RMC CCEP Physician insures that Phase II patients with the following undiagnosed symptoms receive the tests and consultations listed below.

<u>Diarrhea</u>	Abdominal	<u>Headache</u>
GI consult Stool for O&P Stool Leukocytes Stool Culture Stool Volume Colonoscopy with biopsies EGD with biopsies & aspiration	GI consult EGD with biopsy/aspiration Colonoscopy with biopsy Abdominal ultrasound UGI series with small bowel FT Abdominal CT Scan	MRI - head LP (glucose protein, cell count, VDRL, oligoclonal myelin, basic protein, pressure) Neuro consult
Muscle Aches /Numbness EMG/NCV	Memory Loss (Only if verified by psych evaluation) MRI - Head Lumbar Puncture Neuro consult Neuro Psych Testing	Vertigo/ Tinnitus Audiogram ENG BAER

Chronic Fatigue

Polysomnography & MSLT

Chronic Cough/SOB	Chest Pain/Palpitations	Skin Rash
Pulmonary Consult Pulmonary Function Tests with Exercise & ABG Methacholine Challenge if PFTs are Normal Consider Bronchoscopy with biopsy/lavage	ECG Exercise Stress Test Holter Monitor	Dermatology consult Consider biopsy

Reproductive Concerns

Urology consult GYN consult